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# Treatment of Recurrent Staphylococcal Mediastinitis: Still a Controversial Issue

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*Background.* **Although surgical management with early debridement and closed mediastinal irrigation has proved successful in reducing early mortality following poststernotomy deep sternal wound infection, recurrence rates are still up to 20%. This study compared the effectiveness and safety of wound dressing with granulated sugar versus early muscle flap surgery in the management of recurrent postoperative Staphylococcal mediastinitis.**

*Methods.* **Between January 1995 and January 2002, 25 patients with severe recurrent staphylococcal mediastinitis were treated with granulated sugar wound dressing (group A) or with wound debridement, v-shape sternectomy and associated muscle flap surgery (group B). Clinical outcomes and perioperative data were analyzed. Outcomes were compared between the groups evaluating the length of time for normalization of white blood cell (WBC) count and of body temperature and length of hospital stay. Patient characteristics determining best treatment option were identified. Survival and incidence of recurrence at follow-up were also analyzed.**

*Results.* **Study groups proved homogenous as to preoperative characteristics. Complete cure was achieved earlier in group A than in group B (defervescence: $p = 0.0005$; WBC normalization: $p = 0.0001$, respectively). Hospital stay was shorter in group A. A statistically significant difference was found in hospital mortality (16% overall) between the two groups with better outcomes in group A ($p = 0.039$). In the patient subset with the most severe preoperative profile (hemodialysis, tracheostomy, inotropic support) surgical treatment produced worse results than the sugar dressing method ($p = 0.048$). No case of recurrence was observed.**

*Conclusions.* **Both treatments proved effective in recurrent type IV A Staphylococcal mediastinitis. Granulated sugar proved a safer option in severely compromised patients.**

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Despite advances in surgical techniques, identification of predisposing factors and antibiotic prophylaxis the incidence of mediastinitis after cardiac surgery has remained constant throughout the years approaching, in recent reports, 1% rate. Such findings are closely related both to the increase in the number of immunocompromised patients undergoing cardiac procedures and to the impossibility of modifying chronic preoperative risk factors. Mortality rates vary from 14% to 47%, and hospitalization cost, due to inherently high morbidity, is trebled [1]. Although early aggressive debridement, closed mediastinal irrigation with povidone-iodine (PVI) solution or antibiotics has proved effective in reducing early mortality, mediastinitis still carries a recurrence rate of about 20% or higher [2–4]. Such a recurrence rate is strictly linked to the recently reported shift from gram-negative to gram-positive bacteria among the most common causative pathogens. Indeed Staphylococcal strains and, especially, coagulase negative Staphylococci (CoNS), are emerging [5–7]. Treatment of type IV A mediastinitis (i.e. mediastinitis presenting within 2 to 6 postoperative weeks, independently of the presence of one or more risk factors, after one unsuccessful therapeutic trial) is still controversial. It may be treated by wound debridement, extensive sternectomy and excision of exposed cartilage if necessary, and muscle or omental flap repair [8, 9]. On the other hand, wound dressing with granulated sugar has proved a reasonable and effective option in this patient subset [10, 11]. To the best of our knowledge no study is available so far comparing those two treatment methods. Aim of the present retrospective study was to compare the effectiveness and safety of wound dressing with granulated sugar versus early muscle flap surgery in recurrent Staphylococcal mediastinitis.

## Material and Methods

### *Patients and Definitions*

Between January 1995 and January 2002, 6687 open heart surgery operations were performed through a median sternotomy. Postoperative mediastinitis developed in 75

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patients (1.12%). A staphylococcal etiology was found in 61.3% of cases. Deep sternal wound infection (DSWI) was defined according to the guidelines of the Center for Disease Control and Prevention [12]; diagnosis of DSWI required at least one of the following criteria: (1) an organism was isolated from culture of mediastinal tissue or fluid; (2) evidence of mediastinitis was seen during operation; or (3) one of the following conditions, chest pain, sternal instability, or fever ($>$ 38°C) was present and there was either purulent discharge from the mediastinum or an organism isolated from blood culture or culture of drainage of the mediastinal area. Classification was based on the criteria proposed by El Oakley and Wright [1]. Briefly, in the absence of risk factors mediastinitis was referred to as Type I when presenting within 2 weeks after operation, Type II when presenting at 2 to 6 weeks after operation; in the presence of one or more risk factors Type III A when presenting within 2 weeks after operation; Type III B when presenting at 2 to 6 weeks after operation. Type IV A defined mediastinitis fulfilling the criteria for Type I, II or III when presenting after one failed therapeutic trial; Type IV B after two or more failed therapeutic trials. Type V defined first mediastinitis presenting more than 6 weeks postoperatively.

Surgical treatment of the acute phase of mediastinitis was based on early wound debridement, primary sternal closure and closed mediastinal catheter irrigation. Details of this procedure are reported elsewhere [13].

Staphylococcal infection recurred in 25 cases who constituted the study population. Based on surgeon preference, these patients were treated by wound dressing with granulated sugar (Group A) or wound redebridement and pectoralis muscle flap surgery (Group B).

The primary endpoints of this retrospective analysis were wound healing along with operative and hospital mortality. Secondary assessment comprised recurrence of mediastinitis and definition of patient characteristics most suitable for each treatment option.

### *Management of Infection and Surgical Technique*

Treatment with granulated sugar was started the day following wound redebridement. The wound was daily washed with oxygen peroxide and 5% PVI solution and filled with unsterilized white granulated sugar four times a day until the wound was healed. Cultures from the wound were performed every day while blood cultures were taken whenever body temperature rose above 38°C. Antibiotics were continued, according to in vitro susceptibility of isolates, until cultures from the wound became sterile. Full blood count was checked daily and blood glucose four times a day. Once cultures from the mediastinum became sterile, granulation tissue was evident and white blood count fell to within the normal range, the patients were trained in self-dressing and were discharged. They were then seen in the outpatient clinic twice a week until a completely clean wound was observed. The possibility of plastic reconstruction to complete wound healing was also considered and proposed to the patients. More details on this original protocol are reported by Trouillet and associates [10] and by our previous studies [11–13]. Group B patients underwent a new extensive surgical debridement and total V-shape sternectomy combined with pectoralis muscle flap as originally described by Mathes [14] and by Jurkiewicz [15] and successively modified by Schroeyers and associates [16]. Cultures of mediastinal drainage samples were performed every day and had to be sterile before removal of the suction devices, and withdrawal of antibiotic therapy. Full blood count was checked daily throughout hospitalization and blood cultures were taken whenever body temperature rose above 38°C.

### *Statistical Analysis*

Statistical analysis was performed with SPSS statistical software package (version 10.1, Chicago, IL). Univariate analysis of qualitative data were performed with Ficher's exact-test, whereas quantitative data, reported as mean $\pm$ SD, were compared with the Wilcoxon sum rank test. A $p$ value less than 0.05 was considered statistically significant.

## Results

As reported in Table 1, study groups proved homogeneous as to age, sex, and previous cardiac procedure. There were no differences with respect to preoperative risk factors for mediastinitis. Indeed, the incidences of diabetes, obesity (body mass index [BMI] $>$ 32), smoking, chronic obstructive pulmonary disease (COPD), bilateral mammary artery harvesting, and surgical revision for bleeding were similar in both groups. Microbiological results with the antibiotic resistance pattern of strains isolated are illustrated in Table 2. There was no statistically significant difference between the two groups as to the type of bacteria found in the cultures of materials retrieved during surgical debridement. *Staphylococcus aureus* was isolated in 17 patients while coagulase negative staphylococci were found in 8. None of the study patients developed a polymicrobial infection nor fungal superinfection. Sixty-eight percent of isolated strains proved resistant to methicillin. Table 2 also reveals the preoperative patient profile. The study population included severely ill patients: 8 were on renal replacement therapy, 8 were on inotropic drugs, and 6 undergone a tracheostomy. These highly compromised patients were almost equally distributed among groups. Complete cure of infection was achieved earlier in group A than in group B. Indeed, the time needed to achieve disappearance of fever and a normal white blood count was significantly lower in the first group ($p = 0.0005$ and $p = 0.0001$, respectively). As a consequence, length of hospital stay was shorter in group A. The mean time interval between hospital discharge and complete closure of the wound in group A patients was 53 $\pm$ 11.6 days. Mediastinitis treatment outcome are illustrated in Table 3. In diabetic patients wound dressing with granulated sugar caused only mild increases of fasting blood glucose levels. However such rise was controlled with insulin treatment. There were no surgical deaths. Overall hospital mortality was 16% (4 patients).

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*Table 1. Patient Demographics, Primary Surgical Intervention, and Preoperative Risk Factors*

| | Granulated Sugar (n = 13) | Muscle Flap (n = 12) | *p* Value |
|---|---|---|---|
| Age | 59.4 ± 13 | 59.6 ± 10.7 | 0.50 |
| Male sex | 10 (76.9) | 8 (66.7) | 0.45 |
| Surgical procedure | | | 0.24 |
| Valve replacement | 6 (46.1) | 1 (8.3) | |
| CABG | 6 (46.1) | 9 (75) | |
| Heart transplant | 1 (7.7) | 1 (8.3) | |
| Aortic dissection | 0 | 1 (8.3) | |
| Risk factors | | | |
| Diabetes | 5 (38.5) | 7 (41.7) | 0.59 |
| Obesity (BMI > 32) | 1 (7.7) | 3 (25) | 0.26 |
| Smoking | 5 (38.5) | 7 (41.7) | 0.28 |
| COPD | 1 (7.7) | 3 (25) | 0.26 |
| Bilateral ITA | 1 (7.7) | 2 (16.7) | 0.48 |
| Redo for bleeding | 0 | 1 (8.3) | 0.48 |

Percentages reported in parentheses.

Bilateral ITA = bilateral internal thoracic artery harvesting; BMI = body mass index; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease.

High risk profile was defined by NYHA class III or IV symptoms, need for inotropic support, acute renal failure, or tracheostomy. The relation between high risk profile and mortality is demonstrated in Table 4. All the four deaths of this series occurred in group B ($p = 0.039$) and all belonged to the high risk subgroup. This corresponded to an eighty percent in-hospital mortality rate among the high risk patients treated with muscle flap. Causes of death were: respiratory failure in 2 patients, multiorgan failure in 1 patient, and refractory heart failure in 1 patient.

Follow-up was complete in all patients and averaged 27 ± 16.6 months (range 1.24 to 57.6). All patients discharged from hospital were alive at the time of this report, all with excellent results. Recurrence of sternal infection was not observed in any group. No patient who had been treated by wound dressing with granulated sugar required further surgery for unpleasant movement of the unclosed sternum.

*Table 3. Mediastinitis Treatment Outcome*

| | Granulated Sugar (n = 13) | Muscle Flap (n = 12) | *p* Value |
|---|---|---|---|
| No fever (days) | 4.77 ± 1.36 | 8.33 ± 2.1 | 0.0005 |
| WBC normal (days) | 6.75 ± 1.34 | 10.75 ± 2.76 | 0.0001 |
| In-hospital stay (days) | 34.23 ± 3.4 | 39.5 ± 3.6 | 0.001 |
| Hospital mortality | 0 | 4 (33.3) | 0.039 |

Percentages reported in parentheses.

WBC = white blood cell.

## Comment

The great increase in the number of immunocompromised patients undergoing cardiac procedures and the impossibility of modifying preoperative risk factors dependent on chronic conditions, make it impossible to reduce to zero the incidence of postoperative mediastinitis. The prevalence of such a severe complication in our series is consistent with those reported in the literature. Early aggressive debridement surgery and closed mediastinal irrigation with povidone-iodine solution and antibiotics effectively reduces early mortality. Nevertheless the recurrence rate in published studies is still as high as 20% [1, 3] and reached 26.5% in a large series published in 1991 [2]. The recently reported shift from gram-negative to gram-positive bacteria as causative pathogens is considered the major determinant of this high recurrence rate. Indeed gram-positive bacteria now account for 70% to 80% of occurrences of mediastinitis [1]. In particular, staphylococcal strains and especially methicillin-resistant and coagulase negative staph-

*Table 2. Microbiological Evaluation and Preoperative Patient Profile*

| | Granulated Sugar (n = 13) | Muscle Flap (n = 12) | *p* Value |
|---|---|---|---|
| Time interval operation-DSWI treatment | 15.2 ± 3.2 | 16.4 ± 3.3 | 0.25 |
| Time interval first treatment-recurrence | 17.2 ± 2.4 | 19.1 ± 2.3 | 0.14 |
| Etiologic agents | | | 0.39 |
| St. Aureus | 8 (61.5) | 9 (75) | |
| CoNS | 5 (38.5) | 3 (25) | |
| Meticillin-resistant strains | 9 (69.2) | 8 (66.7) | 0.61 |
| Pretreatment fever (> 38°C) | 8 (61.5) | 9 (75) | 0.39 |
| Pretreatment WBC | 17384 ± 5013 | 14833 ± 3531 | 0.18 |
| NYHA III–IV | 3 (23.1) | 5 (43.7) | 0.29 |
| Inotropic drugs for LCO | 3 (23.1) | 5 (43.7) | 0.29 |
| Hemodialysis for ARF | 4 (30.8) | 4 (33.3) | 0.61 |
| Tracheostomy | 3 (23.1) | 3 (24.9) | 0.41 |

Percentages reported in parentheses.

ARF = acute renal failure; CoNS = coagulase negative Staphylococci; DSWI = deep sternal wound infection; LCO = low cardiac output; NYHA III–IV = New York Heart Association class III or IV; WBC = white blood cell.

*Table 4. Preoperative Patient Profile and Related Mortality in Study Groups*

| | Granulated Sugar (n = 13) | Muscle Flap (n = 12) | *p* Value |
|---|---|---|---|
| Low risk profile (LRP) | 9 (56.3) | 7 (43.7) | NS |
| High risk profile (HRP) | 4 (44.4) | 5 (56.6) | NS |
| Hospital mortality in HRP | 0 | 4 (80) | 0.048 |

NS = not significant.

ylococci (CoNS), are emerging [5–7], being most frequent in deep infections [17]. The well-known ability to adhere to foreign materials, along with production of slime and genetically mediated antibiotic resistance are the most important virulence factors of these strains [18–21]. These reasons explain why recurrence rates can be even twice higher in subgroups of patients with Staphylococcal etiology mediastinitis than those reported in general studies. A recent study by Tegnell and coworkers [7] focusing on CoNS postoperative mediastinitis reported a recurrence in 11 of 33 patients, which compares favorably with the incidence reported in this series. Similarly, the incidence of staphyloccus aureus and of methicillin-resistant isolates in this series was consistent with published data.

Treatment of mediastinitis presenting within 6 postoperative weeks, independent of the presence of one or more risk factors, after one unsuccessful therapeutic trial is extremely difficult and controversial. Controversies are also exacerbated by the lack of uniform definitions and classifications of mediastinitis in published series which makes it difficult to compare the outcome and adequacy of different strategies. Aggressive wound debridement (sternectomy with or without the excision of exposed cartilage), associated with muscle or omental flap repair has proved to be a major advance [8, 9]. Immediate application of muscle flap or secondary treatment after a period of wet dressing is still debated, even though both strategies [8–14] resulted in good healing and low recurrence rate. In studies comparing flap surgery with debridement and open granulation [1, 22] the length of the hospitalization in those patients undergoing the granulation strategy was longer.

Other concerns derive from patient selection. In particular, the applicability of muscle flaps in patients with multiorgan failure has not yet been demonstrated. A recent report by Schroeyers [16], although proving the efficacy of muscle flaps, has pointed out that this strategy should be reserved for patients in good hemodynamic conditions. Similar evidence has come from the data reported by Grossi and coworkers who focused on preoperative metabolic condition [22]. A recent study by Combes and associates [23] compared the outcomes of patients who developed mediastinitis during an otherwise uneventful postoperative course with those of patients admitted for severe postoperative organ failure and subsequently developing mediastinitis: despite similar response to treatment, survival was significantly lower in the second group.

In our experience, primary flap surgery in recurrent mediastinitis has proved effective in wound healing and in preventing recurrence. Nevertheless, mortality following flap surgery was higher and patients with worse pretreatment profile had poorer outcomes.

Treatment of infection by wound dressing with honey and molasses has been used throughout history dating back to the ancient Egyptians. Recently Herszage and colleagues reported a cure rate as high as 99.2% in a series of 120 patients with infected wounds treated with simple granulated sugar [24]. The scientific basis for this efficacy is still under investigation. Some reports focused on bacterial growth inhibition due to lowered water activity in the wound [25, 26]. Other studies favored a less specific mechanism, stressing the importance of osmotic shocks [10]. Neoangiogenesis stimulating properties of polysaccharides have also been suggested [13]. A well-known study by Trouillet and coworkers on a series of 19 critically ill adults with acute mediastinitis treated with granulated sugar included 8 patients affected by recurrence after continuous irrigation. Staphylococcal strains were the causative agents in 70% of the cases. Although 75% in this subgroup were on inotropic or vasoactive drugs and 50% needed prolonged ventilation, there was just one death, not related to wound complication and no treatment failure. Such results compare favorably with those reported in our series: no deaths and no recurrence despite the need for inotropic support, or prolonged mechanical ventilation or hemodialysis in 4 patients. Thus our data demonstrate the efficacy and the superior safety of this less invasive treatment option.

The present study was retrospective and patients were allocated to treatment group according to the surgeon's choice; moreover, despite the adequate statistical power of the tests employed the number of patients in each group is small. This is clearly due to the single center design of the trial itself, which, on the other hand, along with the shortness of the study time period, is a guarantee of the uniform perioperative selection and management of the patient population throughout the experimentation.

In conclusion, the results of the present retrospective comparison between wound dressing with granulated sugar and muscle flap surgery prove that both strategies are effective in the treatment of Type IV A Staphylococcal mediastinitis as regards wound healing and prevention of further recurrence. Granulated sugar is a safer option in severely ill patients.

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